

regimen may also be implemented where donor specific blood transfusion are performed 12 days prior to transplant to trend towards tolerance (Koshiba T, Li Y, Takemura M, Wu Y, Sakaguchi S, Minato N, Wood K J, Haga H, Ueda M, Uemoto S. *Transpl Immunol* 2007 February; 17(2):94-7; Jovanovic V, Lair D, Soullillou J P, Brouard S. *Transpl Int.* 2008 March; 21(3):199-206. Epub 2007 Dec. 5. Review. Several rat models for the administration of NKA prototypes are possible. One model is the allotransplant model wherein using the inbred rat strain DA (d=d blood group, A=agouti) donors to rat strain Wistar-Furth (WF) (strong histocompatibility).

[0675] 1. MHC compatible pairs: Fisher rat strain (F344) to Lewis rat strain (LEW)

[0676] 2. ZSF rat:

[0677] a. Generated from the first-generation (F1) offspring of the spontaneously hypertensive shhf (severe hypertension & heart failure) rat×Zucker Diabetic Fatty (ZDF) rat.

[0678] i. Obese, diabetic, hypertensive; proteinuria

[0679] ii. Offspring of the ZDF×SHHF are syngeneic in litter

[0680] 1. Half the offspring are obese+disease; other half are lean

[0681] iii. F1 offspring can accept transplants from parent SHHF and ZDF strains

[0682] 3. Allogeneic donor options

[0683] a. Original lean Zucker Fatty rat (ZF)—an out-bred strain

[0684] b. Parent strain of the ZF—the Wistar

[0685] 4. ZSF1 and SHHF testing with RT1.B and RT1.D (Major Histo Compatibility Class II assays)

[0686] a. ZSF1—L/K haplotypes

[0687] b. SHHF—K haplotype

[0688] Experimental Design

[0689] Methodology—injectable cells

[0690] 1. Control and autologous arms

[0691] a. ZSF no transplant; no immunosuppression (n=3)—Pure control

[0692] b. ZSF no transplant; with immunosuppression (n=3)—Med effect

[0693] c. ZSF with empty vehicle; with immunosuppression (n=3)—Med effect and vehicle impact

[0694] d. ZSF to ZSF; no immunosuppression (n=5)—Cell effect; no med component

[0695] e. ZSF to ZSF; with immunosuppression (n=5)—Med effect with procedure

[0696] 2. Allotransplant Experiments

[0697] a. Wistar to ZSF (or lean Zucker to ZSF); with immunosuppression (n=5)—Med effect on allotransplantation model

[0698] b. One or more of the following immunosuppressive regimes would be implemented in conjunction with delivery of the allogeneic cells:

[0699] i. Cyclosporin A (CsA) (10 mg/kg) daily by gavage

[0700] ii. Tacrolimus (0.2 mg/kg) daily by gavage (2nd choice)

[0701] iii. Rapamycin (1 mg/kg) daily by gavage (1st choice)

[0702] iv. Mycophenolate Mofetil (10 mg/kg) daily by gavage

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